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MANAGEMENT OF ACUTE RENAL FAILURE*

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DIETARY TREATMENT

DIETARY treatment is of great importance in all cases of acute anuria not only in acute glomerulonephritis,[1] but also in lower nephron nephrosis.[2, 3, 4] During the last fifty years the treatment of acute nephritis has varied considerably. Until forty years ago every case of acute nephritis was treated with an absolute milk diet. Large quantities of milk, three to four liters daily, were advocated because the fluid allegedly flushed the glomeruli and tubules and kept the urinary passages open. Milk was considered to be especially appropriate for this purpose because it was so bland a nutrient that it could not irritate the kidneys. Finally, the milk diet assured a satisfactory caloric intake. All this changed when in the first decade of the twentieth century Strauss from Berlin and Widal from Paris both demonstrated that in the serum of uremic patients, the non-protein nitrogen and the urea nitrogen content was always increased. A few years later Widal emphasized the importance of the sodium chloride intake for the formation of the edema.

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As milk contains large amounts of proteins (35 gm. per L.) and sodium chloride (2.5 gm. per L.), both of which were detrimental for patients with acute nephritis, the classical milk diet was abandoned and a diet poor in protein and poor in sodium chloride was advocated. Shortly after the first World War Volhard[5] recommended an absolute starvation diet consisting only of 800 cc. of fruit juice for patients with acute glomerulonephritis. In his opinion recovery of the diseased renal parenchyma required absolute rest and for this purpose not only excretion of chlorides, urea and other substances but also of water had to be restricted as much as possible. After the introduction of this starvation diet cases of anuria and of eclampsia in acute nephritis have become extremely rare.

In the last decade the unfavorable side actions of the starvation diet have been emphasized. Insufficient intake of calories increases the catabolism of body proteins which in its turn leads to an increase of the non-protein nitrogen of the blood. On a starvation diet so much body protein is broken down that from this source alone 20 grams of urea are formed daily. Thus in cases of impaired renal function starvation produces enough urea to cause a rise in the blood urea nitrogen of 20 mg. per cent daily in an adult. This is the reason why many clinicians now attempt to avoid starvation. As proteins and salts should be avoided, Borst[6] has advocated a daily diet consisting of 200 grams of butter and 200 grams of sugar. The butter is first melted, then carefully mixed with the sugar and about 12 grams of flour and some coffee flavor are added. The whole is put into the refrigerator. A teaspoonful of this mixture given in iced condition is palatable, but most patients complain if they have to take 400 grams of this mixture daily. Only patients who have been persuaded to understand the necessity of such a diet may be able to tolerate it. On this diet the body produces only four grams of urea daily. Borst calculates that a patient with no kidney function should live five times as long on such a regime as on a starvation diet. It should also be remembered that toxic substances like potassium which play an important role in uremia, are derived from the endogenous break-down of protein.

Even the Kempner diet[7] (rice, fruit and sugar) consisting of 460 grams of carbohydrates, 20 grams of protein, 0.2 grams of sodium and 0.15 grams of chloride could be used although it contains more protein than the mixture of butter and sugar as advocated by Borst.

After the most serious dangers have been overcome by the butter-sugar or the starvation regime, a diet providing 2,480 calories with four grams of nitrogen, 1,280 mg. of potassium and 470 mg. of phosphorus has been advocated.

Potatoes (boiled)	100 gms.
Rice, Polished (raw)	50 "
Flour (80%)	100 "
Custard powder	25 "
Cream (20%)	200 "
Butter	100 "
Sugar	100 "
Apples or pears	200 "
Vegetables	100 "
Cocoa powder	10 "
Tea infusion	500 "
Coffee infusion	100 "

As far as our own results are concerned, the following figures may be of some importance. Between April 1943 and December 1944, eleven patients with acute nephritis were treated with low salt diet and fluids ad libitum. One patient died. Between December 1944 and August 1948, nine patients with acute nephritis were treated with a starvation diet of 800 cc. of fruit juices for about one week. Thereafter, low salt, low protein diet was given. Of these patients, two died. It is true that nearly all these patients had already been suffering from acute nephritis for several weeks previous to admission to the Hospital. As a rule, no dietary measures at all had been ordered during this period. Under these circumstances, the treatment of the acute nephritis had to start at a stage when in some cases irreparable changes had already occurred. In any case, the difference between the starvation diet and the more liberal low salt, low protein diet do not seem significant.

The introduction of a starvation diet emphasized for the first time the importance of the restriction of the fluid intake in oliguric or anuric patients, irrespective of the etiology of the renal failure. The ingestion of large amounts of fluid in such cases will easily lead to overloading of the circulation with ensuing lung edema and anasarca.[8] A liberal ingestion of sodium chloride will favor the development of these dangerous complications still more. In anuria the fluid intake should not exceed 1,000 cc. per day which is sufficient to balance the normal loss of water through skin and respiratory tract. In case vomiting and diarrhea are present, the water intake should be adequately increased. Ingestion

of NaCl may be necessary if chlorides are lost in the vomitus. Acidosis should be combatted with sodium bicarbonate by mouth. In case intravenous treatment of the acidosis is necessary small amounts of 5 per cent sodium bicarbonate solution are preferable because they contain as much base as large quantities of 1/6 mol. sodium lactate solution. The outlook of anuria whether due to acute nephritis or lower nephron nephrosis will be improved considerably if from the beginning a low sodium chloride, low protein diet with restricted fluid intake or a starvation diet of 800 cc. of orange juice or a butter-sugar diet, is prescribed.

Occasionally cases of oliguria or anuria are encountered where dietary treatment alone does not lead to favorable results. Many such patients are admitted with left heart failure and pulmonary edema because in order to bring about diuresis they have been overloaded with fluid and salt. (Leiter *et al*[8a] Muirhead and Fromm[8b]). Often they are also in severe acidosis or alkalosis. In order to treat such cases methods have been perfected recently by which, at least temporarily, large quantities of the toxic substances which accumulate in the blood during anuria can be removed. These methods consist of continuous dialysis of the blood either by way of an artificial kidney or by continuous lavage of the peritoneal cavity or even of the intestine. Recently exsanguinotransfusion has been recommended. These methods are applied in the hope that by cleansing the blood of the anuric patient life can be prolonged until the tubules have regenerated and diuresis has been restored. The greatest experience has been collected with the artificial kidney as popularized by Kolff[9] and with peritoneal dialysis as revived by Fine, Frank and Seligman.[10] Both methods use the same principle. In the artificial kidney the blood is dialyzed in a cellophane or cellulose-acetate tube; in the peritoneal dialysis the peritoneal membrane is used as a dialyzing membrane. Intestinal irrigation and exsanguinotransfusion are other methods for the treatment of acute anuria which are based upon fundamentally different principles.

Artificial Kidney

History: Abel[11] and his co-workers already in 1913 constructed an artificial kidney. They prevented the coagulation of blood by hirudin and dialyzed the blood by letting it run through celloidin tubes which were submerged into a dialyzing fluid. Haas[12] between 1915 and 1928 followed up these experiments using celloidin tubes. He also started

with hirudin but soon recognized that for the dialysis of human blood, heparin had to be used. He actually dialyzed the blood of two uremic patients. Necheles[13] in 1923 used tubes made of peritoneal membrane and Thalhimer[14] in 1938 cellophane tubes. Both these investigators performed dog experiments only. The first apparatus which could be readily used on patients was constructed by Kolff in 1943.[9] He could obtain practical results because he could use 1.) Cellophane or the closely connected cellulose acetate (Visking), 2.) Heparin, 3.) A large dialyzing surface, 4.) A dialyzing fluid of correct composition.

Table I shows the differences between the Kolff kidney and its predecessors. Slight modifications of Kolff's apparatus have been published.[15, 16] Other artificial kidneys have been constructed[17] and the models devised by Murray[18] and by Alwall[19] have actually been used in humans (Table I).

Different investigators used dialyzing solutions of different composition. As brought out by Abel plasma only contains 0.6 per cent of chloride and 0.9 per cent of sodium. If the bathwater contains more chloride than the plasma absorption of excessive amounts of chloride ions takes place. This explains why the use of 0.9 per cent sodium chloride as the dialyzing fluid easily leads to anasarca and pulmonary edema. Kolff's dialyzing fluid (Table II) contains 0.6 per cent NaCl, 0.4 per cent KCl, 0.2 per cent of $NaHCO_3$, and 1.5 to 2 per cent of glucose, that is, 383 mg. per cent of chloride (plasma water 370 to 420 mg. per cent), 291 mg. per cent Na (plasma water 340 to 360 mg. per cent), 21 mg. per cent K (plasma water 18 to 22 mg. per cent), and 53 volume per cent of CO_2 (plasma water 55 to 77 volume per cent). The bathwater does not contain calcium because this would be precipitated by the sodium bicarbonate. It follows that during the dialysis in the artificial kidney the blood loses considerable amounts of calcium and calcium gluconate must be repeatedly injected intravenously during the procedure.

Glucose is added in order to make up for the osmotic pressure of the plasma proteins. In patients with edema the glucose withdraws fluid from the blood plasma. At the same time glucose absorbed from the dialyzing fluid into the blood has a definite caloric value. On the other hand, the blood sugar of the patients rises to very high values and in the future this excess of glucose may have to be replaced by a non-dialyzable colloid substance. Until now this has not been possible.

TABLE I—HISTORY OF THE DEVELOPMENT OF THE ARTIFICIAL KIDNEY

Investigator	*Material*	*Surface*	*Anticoagulant*	*Capacity*
Abel et al.[11] 1913	Celloidin	3,200 sq.cm.	Hirudin	20 gms. NPN in 112 hrs.
Haas[12] 1915-28	Celloidin	2,160 sq.cm.	Hirudin Heparin	2.7 gms. NPN in 7 hrs.
Necheles[13] 1923	Tubes of peritoneal membrane	4,000 sq.cm.	Hirudin	
Thalhimer[14] 1938	Cellophane	4 tubes of 2 x 30 cm.	Heparin	200-700 mgms. BUN in 3-5 hrs.
Kolff[9] 1943-44	Cellulose (Viking)	33-50 yds. 20,000 sq.cm.	Heparin	42-141 gms. BUN in 8 hrs.
Murray[18] 1947	Cellulose (Viking)	12 yds.	Heparin	6.6 gms. NPN in 8 hrs. 49 gms. NPN in 26 hrs.

TABLE II—COMPARISON OF ELECTROLYTES IN PLASMA AND DIALYZING FLUIDS

	Plasma Water	*Kolff[9] Artificial Kidney*	*Kolff & Kop Peritoneal Dialysis[22]*	*Tyrode Solution*
Na mg.%	313-330	291	291	343
Cl mg.%	340-393	383	383	502
K mg.%	16-20	21	21	11
CO_2 vol.%	55-77	53	53	27
Ca mg.%	10	—	10	7
Glucose mg.%	100	2,000	2,000	100 plus traces of P and Mg.

Whereas Bywaters and Joekes used the dialyzing solution as recommended by Kolff, Murray dialyzed against a solution containing 0.8 per cent of NaCl, 0.02 per cent of KCl, 0.02 per cent of $CaCl_2$, 0.01 per cent of $MGCl_2$, 0.1 per cent of $NaHCO_3$ and 0.1 per cent of glucose. Theoretically this solution contains an excess of chloride ions (Table II). Alwall used 0.9 per cent NaCl as dialyzing fluid.

Results: Kolff has treated thirty-one patients, five of whom survived. Two of the five survivors suffered from acute glomerulonephritis, three from lower nephron nephrosis (hepato-renal syndrome after cholecystitis, mercury poisoning and sulfa-drug anuria). In his opinion, dialysis in the artificial kidney is indicated if the blood urea nitrogen has increased to 160 mg. per cent or if the potassium content of the blood has gone up or if severe acidosis has developed. The dialysis lasts usually between five and fourteen hours. During this period so much urea is removed from the blood that the blood urea nitrogen goes down to 50 or 60 mg. per cent. At the same time considerable quantities of creatinine, uric acid, indican, xanthoprotein products are cleared from the blood and can be recovered from the bathwater.

Two of the ten patients treated by Bywaters and Joekes[15] survived. One patient developed oliguria after an explosion and the urea nitrogen of the blood had gone up to 180 mg. per cent. Three days after the dialysis, diuresis started. The second patient became severely uremic after an operation under myanesin anesthesia, probably due to hemolysis caused by the anesthetic. In this patient uremia developed, although he excreted daily about one liter of urine. On the 26th day after operation the blood urea nitrogen had risen to 200 mg. per cent and the artificial kidney was used. Nine days after dialysis, the urinary output increased considerably and the patient recovered. Two of the patients treated with Murray's artificial kidney survived.[18] The first one was a woman of 26 years who after an abortion developed anuria. On the ninth day the patient was treated with the artificial kidney for one hour, two days later for eight hours and again three days later for seven hours. The patient improved and two days later diuresis set in. The other patient, 40 years old, received a transfusion with incompatible blood. After nine days of anuria she was deeply uremic. Treatment with the artificial kidney for 6 hours resulted in a great improvement. Next day diuresis started and the patient recovered. Table III gives a review of the reported cases of recovery after dialysis in the artificial kidney.

TABLE III—CASES RECOVERED AFTER DIALYSIS IN ARTIFICIAL KIDNEY RECORDED IN THE LITERATURE

Diagnosis	*Anuria*	*Dialysis*	*Blood Urea Nitrogen Mg.%*		*Diuresis After Dialysis*
			Before	*After*	
Hepatorenal syndrome[9]	8 days	111 hrs. 80 L 60 gm.U+	190	58	2 days
13 yrs. Acute Nephrosis[9]	7 days	4½ hrs. 34 L 45 gm.U+	120	65	1 day
54 yrs. Acute Nephrosis[9]	5 days oliguria	5 yrs. 60 L 66 gm.U+	150	80	2 days
50 yrs. Sulfa drugs[9]	4 days	51 L 52 gm.U+	100	49	2 days
23 yrs. $HgCl_2$[9]	7 days	39 gm.U+	174	69	3 days
31 yrs. Crush syndrome[15]	8 days 150 cc.	5 hrs. 21 L 32 gm.U+	180	100	3 days
52 yrs. Postoperative (myanesin hemolysis)[15]	26 days (output 1 L daily)	41 hrs. 19 L 38 gm.U+	200	120	9 days
26 yrs. Abortion[18]	9 days (output 35 cc. daily)	1.8, 7 hrs. 6.7 gm. NPN	120 NPN	65 NPN	3 days
40 yrs. Transfusion reaction[18]	8 days	26 hrs. 49.4 gm. NPN	179 NPN	100 NPN	1 day

TABLE IV—TWO MOUNT SINAI HOSPITAL CASES RECOVERED AFTER DIALYSIS IN ARTIFICIAL KIDNEY[20]

Diagnosis	*Anuria*	*Dialysis*	*Blood Urea Nitrogen Mg.%*		*Diuresis After Dialysis*
			Before	*After*	
25 yrs. $HgCl_2$	5 days	6 hrs. 50 gm. U+	150	70	7 days
		1st dialysis			
30 yrs. CCl_4	9 days	6 hrs. 34 gm. U+	108	54	
		2nd dialysis			
	15 days	6 hrs. 41 gm. U+	85	35	2 days after 2nd dialysis

Alwall has treated five patients, three with acute and chronic nephritis, one with polycystic kidney and one with a carcinomatous obstruction of the ureters. In all patients the urea and other nitrogenous waste products which had accumulated in the blood were reduced considerably. All felt better after the dialysis but they died shortly thereafter from the original disease.

At the Mount Sinai Hospital six patients with anuria have been treated with the Kolff kidney (Fishman *et al*[20]). Four were in the last stages of uremia and died shortly after the dialysis. The two last patients were in better shape before the treatment started and recovered after dialysis (Table IV).

The first patient was a woman, 25 years of age, who had introduced 2.5 grams of mercury bichloride in tablets into the vagina. She was admitted on the fifth day of the anuria and only then was BAL treatment started. She had extensive necrosis of the mucous membranes of the mouth and vagina. The hemoglobin had gone down to 8.5 grams and the general condition was very poor indeed. The blood serum contained large amounts of urea and other nitrogenous products, the carbon dioxide combining power was 26 volume per cent.

On the night of admission dialysis with the artificial kidney was performed. The injection of 250 mg. of heparin proved to be sufficient to keep the clotting time of the blood between one and four hours during the six hours the dialysis lasted. The dialysis resulted in the removal of 24 grams of urea nitrogen, 6.7 grams of uric acid, 9.7 grams of creatinine and 6.5 grams of protein. At the end of the dialysis the non-protein nitrogen of the blood had diminished from 150 mg. per cent to 70 mg. per cent, the urea nitrogen from 116 mg. per cent to 30 mg. per cent, the uric acid from 14 mg. per cent to 6.9 mg. per cent, the creatinine from 14.1 to 5.7 mg. per cent, the inorganic

phosphorus from 7 to 1.5 mg. per cent. During the dialysis the general condition of the patient improved considerably. Nevertheless, the following days were critical because of severe vomiting and diarrhea. The urea nitrogen rose again notwithstanding a gradual increase of the urinary output. On the seventh day after dialysis the quantity of urine approximated the intake of fluid. However, only when the diuresis increased to several thousand cc. and the urea nitrogen concentration of the urine approached 400 mg. per cent, did the nitrogenous retention products begin to disappear from the blood. During this period a diet high in carbohydrate, high in fat and with extreme limitation of protein was given. The intake of fluid was restricted to about one liter for every 24 hours. On an average daily approximately 4 grams of sodium chloride and 16 grams of sodium bicarbonate were given by mouth, depending upon the chloride content and the carbon dioxide combining power of the serum. Ultimately, the renal function returned to normal.

The second patient was a man of 30 years who for five hours had been exposed to fumes of carbon tetrachloride. Seven days after the intoxication the patient became completely anuric. On the eighth day he was admitted to the Mount Sinai Hospital. He was severely uremic, with high nonprotein nitrogen (170 mg. per cent) and acidosis (carbon dioxide combining power of 28 volume per cent). On the second day after admission the patient was treated with the artificial kidney for six hours. The injection of 250 mg. of heparin resulted in a satisfactory retardation of the clotting. During the dialysis 34 grams of urea, 3.8 grams of uric acid, 12.4 grams of creatinine, 4.1 grams of inorganic phosphorus and 8.3 grams of protein were removed. The blood urea nitrogen came down from 108 mg. per cent to 54 mg. per cent, the uric acid from 11.3 mg. per cent to 8.3 mg. per cent, the inorganic phosphorus from 4.1 mg. per cent to 3.1 mg. per cent. Extreme oliguria persisted and the nitrogenous waste products accumulated again in the blood. Six days after the first dialysis he was treated for the second time with the artificial kidney for six hours. During the dialysis 41 grams of urea, 3 grams of uric acid, 16.7 grams of creatinine, 2.7 grams of inorganic phosphorus and 22 grams of protein were removed. The blood urea nitrogen came down from 85 mg. per cent to 35 mg. per cent, the uric acid from 5.6 mg. per cent to 2.5 mg. per cent, the creatinine from 27.2 mg. per cent to 19.8 mg. per cent, the inorganic phosphorus from 7.5 mg. per cent to 3 mg. per cent. Two days later, diuresis set in which resulted in a gradual recovery.

The clinical course in this case was characterized by freedom from uremic manifestations despite a long period of renal insufficiency and the accumulation of large amounts of urea and other retention products in the serum.

Everytime a patient with anuria and uremia recovers after treatment with the artificial kidney, the question can be raised as to whether this patient would not have recovered spontaneously. This holds true especially for patients who are no longer completely anuric and where oliguria has already replaced the anuria. During the first weeks after diuresis has started, retention of urea and other catabolic products in the blood may still be progressive. As long as the urea concentration in the urine is less than 400 mg. per cent the urea nitrogen and the non-protein nitrogen of the blood continue to increase. It may be advisable to dialyze such an oliguric patient in order to relieve the blood from the excess of waste products, but in such cases the artificial kidney can hardly be considered to have acted as a life-saving device. The difficul-

TABLE V—PERITONEAL DIALYSIS

Animal Experiment

1923	Putnam	Cats	Intermittent
1923	Ganter	Guinea pigs	Intermittent
1925	Lanzberg & Gnoinski	Guinea pigs	Intermittent
1926	Rosenak & Siwon[21]	Dogs	Continuous
1927	Heusser & Werder[23]	Dogs	Continuous
1932	Bliss, Kastler & Nadler	Dogs	Intermittent
1932	Von Jeney	Dogs	Continuous
1932	Von Haam & Fine	Rabbits	Intermittent
1946	Abbott & Shea	Dogs	Intermittent
1946	Seligman, Frank & Fine	Dogs	Continuous

ties encountered in the appraisal of such cases are clearly demonstrated by the following patient.

Three days after exposure to carbon tetrachloride a patient developed anuria. After the anuria had lasted for three days, diuresis started. Unfortunately, he then was treated with large amounts of fluid and saline so that when ten days after the intoxication he was admitted to The Mount Sinai Hospital, left heart failure had set in. In the Hospital the daily diuresis gradually increased. On the first day of admission it was only 260 cc., on the sixth day of admission, that is, 16 days after the intoxication, it had risen to 1605 cc. Notwithstanding this apparently satisfactory output, the urea nitrogen of the blood had increased progressively to 212 mg. per cent. Patient was irrational and heart failure still persisted. The outlook seemed hopeless. On the night of the 16th day, the patient would have been dialyzed were it not that the artificial kidney was out of order. In the next days the diuresis increased rapidly and the patient recovered spontaneously. Nine days later the blood urea nitrogen was only 28 mg. per cent.

Summarizing it must be pointed out that no certain conclusion can be reached as to whether dialysis by the artificial kidney is actually a life-saving device. At the same time, in the eleven patients who recovered the artificial kidney seems to have had a favorable influence upon the course of the disease. Thus the circumstantial evidence appears

to be in favor of the opinion that dialysis in the artificial kidney results in temporary improvement which may perhaps make survival possible until restoration of the renal function sets in.

Peritoneal Dialysis

History: As in a real dialyzer substances travel from the peritoneal cavity to the blood and in the reverse direction, with the exception of colloids. Table V shows that the method of peritoneal dialysis has been developed gradually and is based upon a long series of experiments. The first experiments with continuous peritoneal dialysis were done by Rosenak and Siwon.[21] After intraperitoneal injection of a solution which is similar in ionic concentration and in osmotic pressure to plasma, no change in the composition of either the peritoneal fluid or plasma occurs. Solutions used for peritoneal dialysis should therefore contain not more than 0.6 per cent of sodium chloride (Table VI).

Seligman, Frank and Fine[10] calculated from their dog experiments that if 1.8 to 3 liters of fluid flow through the abdominal cavity per hour, a urea clearance of 12 to 16 cubic centimeters of blood per minute is obtained. Later Kolff and Kop[22] found in humans that when the inflow of the dialyzing fluid into the peritoneum is kept at one liter per hour, a urea clearance of eleven centimeters of blood per minute results. These figures agree very satisfactorily. It follows that removal of catabolic products from the blood by peritoneal dialysis is equivalent to 40 to 75 per cent of the clearing capacity of the kidneys.

The amount of urea and nitrogen derivatives which can be removed from the blood of uremic patients by peritoneal dialysis of three days duration varies between 20 and 60 grams. In one case Kolff and Kop even removed 300 grams of urea. During the dialysis the urea content of the dialyzing fluid goes up to about 50 per cent of the urea content of the blood.

Results: Table VII shows the increase of popularity of peritoneal dialysis as a clinical method in this part of the world since the publications of Seligman, Frank and Fine.[10]

In 1927 Heusser and Werder[23] reported experiments with intraperitoneal dialysis on dogs. In the same article they mention briefly, in passing, that they also treated three uremic patients with continuous peritoneal dialysis. The results were not favorable evidently, because not enough fluid passed through the peritoneal cavity.

TABLE VI

	Cunningham and Darrow	*Frank, Fine and Seligman (Tyrode[10])*	*Hartmann*	*Abbott and Shea "A" solution*	*Odel and Ferris and Pearson[21] "P" solution*	*Kolff Artificial Kidney*	*Kolff and Kop.[22] peritoneal dialysis*
NaCl Mg. %	650	800	600	610	600	600	600
$NaHCO_3$ Mg. %	250	100		220	300	200	200
KCl Mg. %	18	20	40	35	20	40	40
$CaCl_2$ Mg. %		10	20	23	10		28
NaH_2PO_4 Mg. %		5		7	5		
$MgCl_2$ Mg. %		10		5	10		
Glucose %		1½		1-2	2	1-3	1-3
Natrium-lactate			240				

Different solutions used for peritoneal dialysis

TABLE VII—PERITONEAL DIALYSIS IN HUMANS

		Cases	*Survived*
1927	Heusser and Werder[23]	3	0
1934	Balasz and Rosenak[24]	2	0
1938	Rhoads[25]	2	0
1938	Wear, Sisk and Trinkle[26]	5	1
1946	Fine, Frank and Seligman[10]	4	1
1946-1948		64	19
	Total	80	21

In 1934 together Balázs and Rosenak[24] published the first complete observations on continuous peritoneal irrigation in two patients with fatal uremia, due to mercury poisoning. In the first case the dialysis lasted only for thirty minutes during which time the peritoneum was perfused with 12 liters 4.2 per cent glucose solution. Only a few grams of nitrogen were removed. The same holds true in the second case where 19 liters of 0.8 per cent sodium chloride solution were used as dialyzing fluid.

Rhoads[25] in 1938 treated two patients with chronic nephritis in the same way. He removed large amounts of urea. The patients reacted favorably but died ultimately from their disease. Wear, Sisk and Trinkle[26] in 1938 treated five patients with continuous peritoneal dialysis. One patient who was uremic and had a stone in the urinary bladder survived. In his case peritoneal dialysis with Locke solution resulted in the removal of 16.4 grams of urea. The non-protein nitrogen of the serum came down considerably, the patient could be operated and recovered. Thus previous to the publication of Fine and associates, twelve patients had been treated with peritoneal dialysis of whom one[26] recovered. Four patients were treated by Seligman, Frank and Fine.[10] One patient with anuria after sulfathiazole medication recovered. This was probably the first patient where the possibility that peritoneal dialysis had worked as a life-saving device could be considered. Since their article more than 68 patients have been treated of whom nineteen recovered.[22, 27-37] Twenty-one of the eighty-one cases published were treated by Kolff and Kop with five survivors.[22] Table VIII mentions the cause of anuria in the patients who survived. Table IX illustrates that success has been obtained even in cases where the composition of the dialyzing fluid was not optimal.

Comparison between the artificial kidney and peritoneal dialysis shows that both methods have their advantages and disadvantages. Heparinization necessary for treatment with the artificial kidney may cause disagreeable hemorrhages during and after the treatment. This danger is greatly decreased since protamine sulphate has become available. Peritoneal dialysis cannot be used immediately after an abdominal operation or when extensive adhesions or peritonitis are present. The artificial kidney is a complicated apparatus which requires adept handling by an expert team whereas the instruments necessary for peritoneal dialysis are simple.

TABLE VIII—RECOVERY AFTER PERITONEAL DIALYSIS

Transfusion reactions	5
Mercury intoxication	4
Sulfathiazole	2
Anuria due to other causes (hyperemesis, prostatism, etc.)	10

TABLE IX—SOLUTIONS USED FOR PERITONEAL DIALYSIS IN 19 RECOVERED PATIENTS

Kolff and Kop solution	5
Tyrode solution	6
Hartmann solution	3
A. solution	2
P. solution	1
0.9% NaCl	1
Locke solution	1
1.8% NaCl	1
Different solutions	1

The fact that Kolff and Kop also used the artificial kidney in six of the twenty-one patients whom they treated with peritoneal dialysis shows that the indications for both methods often run parallel (blood urea nitrogen of about 180 mg. per cent, increased potassium content of the serum or marked acidosis). Other investigators start dialysis in patients with mercury poisoning when the anuria exists for three days. Clinical experience has shown that in such cases the outlook is very serious indeed, even if the urea nitrogen content of the blood has not yet reached a level of 180 mg. per cent.

In every patient with uremia due to anuria who recovers after peritoneal dialysis, the possibility that recovery could have been a spontaneous one has to be considered. In addition the dangers and complications of this method should not be underestimated. Peritoneal infection, difficulties in maintaining a satisfactory flow through the peritoneal cavity,[38] abdominal colic and meteorism are frequently the reason why a dialysis has to be terminated prematurely.

Nevertheless, in some of the twenty patients who recovered after

peritoneal dialysis the method apparently has had a favorable influence upon the course of the disease.

Intestinal Irrigation

Introduction: It is true that by irrigation of the intestine, especially of the small intestine, nitrogenous products can be removed from the blood. However, it seems hardly appropriate to designate intestinal irrigation as intestinal dialysis. Intestinal irrigation cannot be identified with dialysis in the artificial kidney or through the peritoneal membrane. If the dialyzing fluid in the artificial kidney or in the peritoneum is isotonic and isoionic with the plasma, then the quantity of fluid and electrolytes in the artificial kidney or in the peritoneal cavity does not, or hardly changes. In contrast, the intestinal wall has specific absorbing qualities and even from an isotonic and isoionic solution large quantities of salts and water are absorbed. The liberal absorption of water and salts from the intestine irrespective of the composition of the irrigation fluid, is a disadvantage in uremic patients with anuria or oliguria, because it easily leads to anasarca and lung edema. Only a relatively small amount of irrigation fluid can be recovered after intestinal irrigation with isotonic fluids, especially when the irrigating fluid runs in slowly. Thus the concentration of the urea present in the fluid recovered from the intestine is high but the total amount of urea removed is only small.

In order to avoid these disadvantages an isotonic solution of 5 per cent magnesium sulphate has been used for intestinal irrigation in animal experiments. As magnesium sulphate is not, or is hardly absorbed from the intestinal lumen, irrigation with this solution will not lead to absorption of excessive amounts of water or salts. In addition, old experiments (Hamburger[39]) seem to indicate that the resorptive power of the intestinal epithelium is markedly decreased after it has been in contact with magnesium sulphate. However, the question may be raised whether large amounts of magnesium sulphate even in isotonic solution will have an irritating effect upon the intestinal wall. Most investigators have added at least a trace of a magnesium salt to the irrigation fluid.

Irrigation of the Colon: Landsberg and Szenkier[40] in 1930 experimented on the influence of colonic irrigation on the condition of rabbits made uremic by uranium nitrate. They found that after lavage of the colon through an appendicostomy tube about 20 mg. per cent urea nitrogen was present in the irrigation fluid. The blood urea nitro-

TABLE X—COLONIC IRRIGATION

	Irrigation fluid	*B.U.N.*
Landsberg and Szenkier	U.N. 20 mg.%	Unchanged (rabbits)
Kolf: Case 1	U.N. 18 mg.%	60 mg.%
Case 2	U.N. 5 mg.%	190 mg.%
Daugherty, *et al.*	U.N. 7 mg.%	180 mg.% before 118 mg.% after

Creatinine unchanged. Hyperchloremic acidosis and polyuria developed

Removed by irrigation 1.66 gm. N.P.N.
" in urine 19.6 mg. N.P.N. } 6 hrs.

gen of the rabbits, however, did not decrease after colonic irrigation. Pendleton and West[41] who experimented mainly with the removal of urea from the blood by irrigation of the small intestine felt that the colon could also be used for the same purpose.

The evidence available indicates that in patients with uremia, irrigation of the colon does not lead to the removal of significant amounts of urea and other nitrogenous products (Table X). Kolff[9] performed colonic irrigation through an appendicostomy. In the first patient thin feces leaked through the anus and further lavage had to be given up. The urea nitrogen content in the escaping perfusion fluid was 18 mg. per cent as compared with a blood urea nitrogen of 60 mg. per cent. In the second patient the thick tube placed in the rectum was closed off by the sphincter ani, and in this way loss of the perfusion fluid was prevented. Although the blood urea nitrogen was 190 mg. per cent, the perfusion fluid only contained 5 mg. per cent nitrogen. Daugherty and associates[42] also perfused the colon in one patient with uremia through an appendicostomy. The perfusion lasted 64 hours. During this period first 35 liters of P-solution (Table VI), later 5½ liters of a P-solution with reduced sodium chloride (480 mg. per cent), and increased $NaHCO_3$ content (350 mg. per cent) were used. After the irrigation the patient's weight had increased by 6.25 pounds. The serum chloride rose from 92.3 to 118.5 milliequivalent, the carbon dioxide combining power decreased from 22.8 to 15.4 milliequivalent. Thus during the colonic irrigation hyperchloremic acidosis developed and

the experiment had to be stopped because anasarca and lung edema set in. At the same time the amount of nitrogen removed was very small. In 64 hours, 24.5 liters of irrigation fluid could be collected containing in total, 1.66 grams of non-protein nitrogen (7 mg. per cent). The blood urea nitrogen came down from 180 mg. per cent to 112 mg. per cent after irrigation, but the creatinine content of the serum (8-9 mg. per cent) did not change. The decrease of the urea nitrogen content of the blood may have been secondary to the polyuria which set in during colonic irrigation, evidently caused by the absorption of large amounts of fluid from the colon. During the colonic lavage 8.16 liters of urine containing 19.6 grams of non-protein nitrogen were voided. This figure is in sharp contrast to the 1.66 grams removed by the colonic irrigation. The renal elimination of nitrogen even by diseased kidneys exceeds more than ten times the removal of nitrogen compounds by colonic irrigation.

Irrigation of the Small Intestine: Irrigation of the small intestine seems to have given somewhat more encouraging results.

Pendleton and West[41] in 1932 inserted a rubber tube into the middle third of the duodenum and another large tube into the ileum near the ileocecal junction (Table XI). The bowel above and below the two tubes was tied off. Fluids were run in through the proximal tube and left the small bowel through the distal tube.

When normal saline was placed in the small bowel of normal dogs the urea content of the intestinal contents rapidly rose to levels which sometimes even exceeded slightly the blood urea nitrogen. Then nephrectomized dogs were injected intravenously with urea in order to obtain a rapid rise of the urea in the blood. In one dog the urea nitrogen of the blood went up to 265 gram per cent. Five minutes after the introduction of saline into the small bowel, the urea nitrogen of the intestinal content had risen to 25 mg. per cent, after fifteen minutes it was 153 mg. per cent. Two hours after the injection the urea nitrogen of the blood was 290 mg. per cent, of the solution in the intestine 299 mg. per cent. After three hours the blood urea nitrogen had fallen to 245 mg. per cent while the bowel still contained 281 mg. per cent. In order to prevent the absorption of large quantities of water Pendleton and West later used 5 per cent magnesium sulphate solution as irrigation fluid. The urea passed quickly from the blood to the magnesium sulphate solution in the intestine and after a short time the urea of the

TABLE XI—IRRIGATION SMALL INTESTINE IN DOGS

	In Irrigation Fluid	*B.U.N. mg.%*		*Time*	
		Before	*After*		
Pendleton and West	280-290 mg.% U.N.	299	245	3 hrs.	Dogs NaCl 9.9%
Rogers *et al.*	4.3-5.4 gm. N.P.N.	198 190 231	126 112 145	6 hrs.	
Seligman *et al.*	Loop of 10 feet—10% of maximal renal clearance				

blood and bowel contents were equal. After introduction of the magnesium sulphate solution a constant fluid volume was maintained in the intestine. In these animal experiments the magnesium sulphate did not cause any difficulties from bowel irritation.

Fine, Frank and Seligman[10] performed continuous irrigation of an isolated loop of ileum, but could remove only small amounts of urea. They calculated that continuous perfusion of a loop of small intestine of 10 feet long would be necessary in order to obtain a urea clearance of 7.5 cc. of blood per minute, that is, about 10 per cent of the maximal normal renal clearance.

Rogers, Sellers and Gornall[43] placed a thin triple bore rubber tube with a small balloon on the tip in the small intestine of dogs (Table XI). They had to manipulate the tube into position through an abdominal incision. Warm physiological saline was introduced above the inflated balloon and withdrawn through another opening of the same tube several feet higher up. Using 12 to 18 liters of perfusion fluid over a period of about six hours, they were able to reduce the non-protein nitrogen of the serum of nephrectomized dogs considerably. In one case the azotemia was lowered from 198 to 126 mg. per cent. In two other cases from 198 to 112 mg. per cent and from 231 to 145 mg. per cent respectively. The rinsing fluid after perfusion contained 4.3 to 5.4 grams of non-protein nitrogen.

The literature mentions the following patients in whom uremic conditions were treated with intestinal irrigation (Table XII). Kolff[9] irrigated an isolated loop of ileum 40 inches long in a patient with uremia. Each end of the loop was connected with the outside by an

TABLE XII—IRRIGATION SMALL INTESTINE IN UREMIA

	In Irrigation Fluid	*B.U.N. mg.%*		*Time*	*Irrigation Fluid*
		Before	*After*		
Kolff	2.3 gm. U.N.	Unchanged		10 h.	Kolff solution
Daugherty *et al*	4 gm. U.N. in 24 h. (10 mg.%)	155	130	24 h.	P-solution
			150	48 h.	
		(creatinine unchanged)			
Oppenheimer and Rosenak	70 & 110 mg.% U.N.	90	83	5 h.	Modified
		83	46	18 h.	Tyrode solution
Marquis and Schnell		330	121	12 h.	NaCl 0.9% or
			66	24 h.	Glucose 10% or NaCl 0.8% plus $NaHCO_3$ 0.1%
	Creatinine unchanged	49		7 d.	

NaCl 0.9%:—Edema and ascites
Glucose 10%:—acidosis
NaCl 0.8% and $NaHCO_3$ 0.1%—hypokaliemia

ileostomy. The continuity of the remaining ileum was restored by an end to end anastomosis. Infection, followed by cicatrization of both stomas of the loop, rendered perfusion of the isolated loop difficult and lavage was only occasionally successful. The best result was obtained when eight liters of fluid passed through the loop in the course of ten hours. During this time 2.3 grams of urea nitrogen were removed. When the lavage fluid runs in very slowly the return flow is necessarily very small. Under these circumstances, the urea nitrogen of the irrigation fluid may go up to 100 mg. per cent. If the perfusion rate is kept to one liter per hour, about 200 mg. of urea nitrogen can be removed per hour. There is probably no advantage in letting the fluid run much faster. It follows that if irrigation during 24 hours would have been possible, nearly 5 grams of urea nitrogen could have been removed every day. This, together with a diet of only fats and carbohydrates, might well keep a nephritic patient at least temporarily in balance. However, the difficulties of perfusion of the ileum loop in Kolff's patient were so great that definite conclusions could not be reached. Kolff used as perfusion fluid the same solution as he used for dialysis with the artificial kidney (Table VI).

Other clinicians have tried to irrigate the small intestine by using

Miller-Abbott tubes or comparable instruments. It is evident that nausea and vomiting as regularly seen in uremia must be a great hindrance to the intra-nasal introduction of Miller-Abbott tubes. A return tube, small enough to be passed by oral or nasal route will usually be too thin to collect large amounts of the irrigated fluid. Thus, too much fluid remains in the bowel and leads to diarrhea. Repeatedly an appendicostomy has been performed through which the irrigation fluid could be sucked out by a pump. The capacity of an appendicostomy tube is not sufficient to cope with large amounts of irrigation fluid and Daugherty and associates are even suggesting that a cecostomy be performed for this purpose.

Daugherty[42] performed intestinal irrigation in a patient with chronic nephritis. The fluid was introduced via a nasal tube which was pushed into the duodenum. At the same time an appendicostomy was performed through which a tube connected with a suction pump was introduced. In this case, also, the suction through the appendicostomy was insufficient and profuse watery stools were produced. During twelve hours of intestinal irrigation 2,750 cc. of fluid were recovered through a rectal tube and only 300 cc. through the appendicostomy tube. The intestinal irrigation was continued for two days at the end of which the patient died. The urea nitrogen of the serum at the beginning of the experiment was 155 mg. per cent, after one day of irrigation it was 130 mg. per cent, and after two days it was again 150 mg. per cent. The creatinine of the serum was high and did not change, the chloride content of the serum rose slightly from subnormal to normal values. The carbon dioxide combining power remained about the same. In 2,010 cc. of fluid recovered from the rectum 10 mg. per cent of urea nitrogen was found.

Oppenheimer and Rosenak[44] passed a modified Miller-Abbott tube through the nose until it reached the middle part of the small intestine. Over a period of five hours four gallons of a solution containing NaCl 0.669 per cent, KCl 0.004 per cent, $CaCl_2$ 0.013 per cent, Mg. lactate 0.0065 per cent, acid sodium phosphate 0.0005 per cent, sodium bicarbonate 0.15 per cent and glucose 1.5 per cent were introduced. The next day six gallons were given in the course of 18 hours. During this procedure the blood urea nitrogen went down from 90 mg. per cent to 46 mg. per cent. The recovered fluid contained 111 and 70 mg. per cent of non-protein nitrogen. They also experienced difficulty in re-

covering the irrigation solution because too much was absorbed. This may explain the relatively high concentration of the nitrogen content of the fluid recovered. At the same time the patient suffered from diffuse watery diarrhea.

Marquis and Schnell[45] reported a case where at least the technical part of the intestinal irrigation was efficient. After two days of anuria due to ingestion of cleaning fluid the patient became completely comatose. Non-protein nitrogen had risen to 330 mg. per cent. At this time two Miller-Abbott tubes were placed in the small intestine, one in the third portion of the duodenum and the other in the lower part of the ileum. In twelve hours 22 liters of fluid were run slowly through and the non-protein nitrogen of the serum dropped to 121 mg. per cent, twelve hours later it was 66 mg. per cent. In the fluid recovered the non-protein nitrogen went up to 50 mg. per cent. Intestinal irrigation was continued for seven days. Gradually diuresis set in and the intestinal irrigation was continued on a half-time schedule. Ultimately it was discontinued. In the next forty-eight hours the urea nitrogen of the blood rose rapidly from 49 to 103 mg. per cent, and the intestinal irrigation was reinstituted. On the tenth day of intestinal irrigation the patient suddenly died.

During the first twenty-four hours of irrigation with 42.7 liters of normal saline, six liters of fluid were retained and general anasarca set in. Thereafter, 20 per cent glucose was used instead of saline. The edema, ascites and hyperpnea disappeared, but acidosis set in. Ultimately 0.8 per cent sodium chloride combined with 0.1 per cent sodium bicarbonate was used. The decrease of the urea nitrogen of the blood indicates that in this way large amounts of urea were removed. As in the other cases of intestinal irrigation the creatinine content of the serum remained high and did not change. The cause of death in this case may have been due to the removal of large amounts of potassium during the irrigation. On the day before death there were many extra systoles. The potassium content of the serum was determined but the result was reported after the death of the patient. The potassium content was found to be 4.6 mg. per cent instead of 16-19 mg. per cent and the patient may well have died from ventricular fibrillation.

It seems that this is the only case where intestinal irrigation was performed in an efficient way. This must have been due to the fact that *two* Miller-Abbott tubes were introduced. It is evident that in nauseated,

uremic patients such a procedure would be impossible. It seems probable that the authors only succeeded because their patient was comatose and did not resist too much against this heroic treatment. Nevertheless, even this patient pulled out both tubes twice and vomited the proximal tube on one occasion.

Summarizing it seems certain that colonic irrigation is useless as far as the treatment of uremia is concerned. It still has not been proved whether intestinal irrigation of the small intestine has a future in the treatment of uremia and anuria. Table XII illustrates that by this method relatively small amounts of urea are removed. It is probably significant that in the two best cases reported the blood urea nitrogen decreased considerably but the creatinine content of the blood did not. Finally no satisfactory method for efficient intestinal irrigation has been devised yet and dangerous, even fatal complications have been caused by changes of the electrolyte content of the blood.

Exsanguinotransfusion

It has been known for many years that an uremic animal can be kept alive by exchange transfusion. An artery of the uremic animal is connected with the vein of the donor animal, a vein of the uremic animal with an artery of the donor. Formerly, paraffinated cannulae were used, nowadays heparin is injected. This favorable result is evidently due to the replacement of the blood of the uremic animal by normal blood (Nyiri,[46] Thalhimer,[14] Thalhimer, Solandt and Best [47]).

The same principle is used in the exsanguinotransfusion where the total mass of the patient's blood is replaced by an equivalent quantity of normal blood. This method has been used rather extensively in newborns suffering from erythroblastosis fetalis and lately by Bessis and Bernard[48] in adults suffering from leukemia. Very recently at the instigation of Bessis this method has been used to obtain improvement in the condition of uremic patients (Pasteur Vallery-Radot, Milliez and Bessis), and it has been successful in six of seven cases. To illustrate the difficulties connected with the exsanguinotransfusion the case treated by Tzanck and Dausset[49] may be mentioned (Table XIII). They treated a forty-year old patient who had taken 16 capsules each containing 0.5 grams of aspidium filicis maris and 0.05 grams of calomel. The patient, in order to hasten the expulsion of the taenia also took magnesium citrate and sodium bicarbonate. It is well known that it is dangerous

TABLE XIII—INTOXICATION WITH FILIX MAS AND MERCURY TREATED WITH EXSANGUINOTRANSFUSION[49]

Day	*Urinary Output in cc.*	*Blood Urea Nitrogen Mg.%*	*Blood Withdrawn*	*Injected*
7	150	163	4 L 11 gm. U+	3.25 L blood 1.2 L NaCl 0.9%
8			3.65 L 9.6 gm. U+	2.55 L blood 1.00 L NaCl 0.9%
9	175	150	6 L 15.8 gm. U+	4.2 L blood 1.7 glucose 5%
10		153	5 L 14.87 gm. U+	3.5 L blood 1.5 L glucose 5%
11	280	133	5 L 12. gm. U+	3.5 L blood 1.4 L glucose 5%
12	375	130	5.5 L 12.9 gm. U+	3.8 L blood 1.6 L glucose 5%
14	300	151	6 L 16.26 gm. U+	4.2 L blood 1.8 L glucose 5%
15	675			
16	3,000		6 L 9.9 gm. U+	4.2 L blood 1.8 L glucose 5%
		Total.....	41.5 L blood 103.2 gm. U+	29.2 L blood and 12.0 L diluting solution

to take alkaline compounds together with calomel because soluble toxic mercury compounds may be formed. On the seventh day of oliguria the urinary output was down to 150 cc.; the urea nitrogen of the blood up to 163 mg. per cent. Patient was somnolent and showed involuntary muscular contractions. On this day the first exsanguinotransfusion was performed.

Three and one-quarter liters of blood were injected diluted with 1.1 liters of normal saline. The transfusion lasted 19 hours and 11 grams of urea nitrogen were removed with the blood. The next day 3.65 liters of blood containing 9.6 grams of urea were extracted and 2.5 liters of blood diluted with 850 cc. of normal saline injected. The next day another 6 liters of blood containing 15.8 grams of urea were extracted and 4 liters of blood diluted with 1.3 liters of 5 per cent glucose were injected. The blood urea nitrogen remained about 150 mg. per cent. The daily diuresis did not exceed

175 cc. The next day the blood urea nitrogen was 150 mg. per cent, the patient was somnolent and had involuntary muscular contractions. A fourth exsanguinotransfusion was performed. Five liters of blood were withdrawn, containing 14.9 grams of urea which were replaced with the equivalent amount of diluted blood. This operation was repeated on the next two days, 5 liters and 5.5 liters of blood were withdrawn, containing 12 and 12.9 grams of urea respectively. The urea nitrogen of the blood diminished slightly to 132 mg. per cent, the urinary output went up to 280 cc. and 375 cc. per day. Two days later the blood urea nitrogen had increased again to 151 mg. per cent, the daily urinary output did not exceed 300 cc. Another exsanguinotransfusion was performed. With the blood 6.3 grams of urea were withdrawn and 6 liters of diluted blood were injected. Thanks to the injection of 200 mg. of heparin this and the following procedures lasted two to three hours each. Now the output improved to 675 cc. per day. Two days later the eighth and last exsanguinotransfusion of 6 liters was performed. After this operation diuresis set in with a vengeance and amounted to 3 and 4.5 liters per day. The urea concentration of the urine increased gradually. The blood urea nitrogen decreased accordingly and on the twentieth day it was 43 mg. per cent.

During a total of eight exsanguinotransfusions given over ten days, 41.15 liters of blood were withdrawn and 41 liters of fluid were injected, consisting of 29.2 liters of blood and 10.8 liters of saline or glucose. The urea eliminated by the exsanguinotransfusion together with the small amounts of urea eliminated in the urine amounted to 125.9 grams. In this way every day an average of 12.6 grams of urea were removed. This may be the reason why notwithstanding persistent extreme oliguria the blood urea nitrogen instead of increasing, remained at the same level or even diminished slightly.

The advocates of this method emphasize that it has definite advantages over the treatment with the artificial kidney, peritoneal dialysis, and intestinal irrigation (Table XIV). In contrast to the other procedures the exsanguinotransfusion removes all toxic substances whether dialyzable or not, improves the protein, water and electrolyte content of the plasma and does not cause hemolysis.

In addition the French authors are of the opinion that the large quantities of fresh blood injected do not represent a simple substitution treatment. They believe that the blood of the anuric patient, full of toxic retention products, inhibits the functions of different organs. The fresh blood permits a resuscitation of the functions not only of the kidney but also of the other organs as well. Injection of heparin, about 200 mg. per operation, permits shortening of the procedure to two to three hours. On the other hand, the procedure is extremely laborious and quite expensive unless there are many members of the family who are in a position to donate the many liters of blood which are necessary.

TABLE XIV

Replacement Transfusion	*Intraperitoneal dialysis*
1. Withdraws all toxic products including those which are non-dialyzable (hemoglobin, myohemoglobin).	Withdraws only dialyzable products.
2. Replaces the pathological blood by normal blood and re-establishes the normal equilibrium of the body fluids.	Withdraws not only pathological products but also certain useful dialyzable substances.
3. Incidents not serious; accidents caused by irregular agglutinins prevented by necessary precautions.	Peritonitis frequently noted, either of the plastic type by adhesions or of an infectious type (septicemias due to B. perfringens post abortum).
4. Can be repeated as often as needed.	Usually cannot be prolonged for more than 5 days. Difficult to repeat due to the formation of adhesions.
5. Disadvantages: large quantities of blood, sometimes of a rare type must be available. Heparinization necessary.	

There may however be instances where repeated exsanguinotransfusions will enable the anuric patient to survive until spontaneous diuresis sets in.

SUMMARY

The treatment of anuria in acute glomerulonephritis and in lower nephron nephrosis is of great practical importance. Acute glomerulonephritis has a tendency to heal spontaneously and in lower nephron nephrosis regeneration of the tubules always starts after ten days have elapsed. Therefore, everything must be done in order to assure survival of the patient for ten or fourteen days after the anuria has started.

The outstanding measure in the treatment of acute anuria consists of reduction of intake of fluids, electrolytes and proteins. In general, the daily fluid intake should not exceed 800 cc. which is sufficient to compensate for the loss of water via the respiratory tract and the skin. In case water is lost by diarrhea or vomiting the fluid intake should be increased. A diet of 800 cc. of fruit juice can be used at least for a

short time. It may be advisable to increase the caloric intake by ingestion of fat and carbohydrate. During hunger considerable amounts of protein are broken down which give rise to the formation of extra urea and other nitrogenous metabolites. For this reason, Borst has advocated a diet consisting of 200 grams of butter and 200 grams of sugar. This diet might well be helpful were it not that for most of the patients the mixture is highly unpalatable. In nearly all cases of anuria intravenous injections of large quantities of fluids and salts are contraindicated. In hypochloremia sodium chloride should be given, in acidosis bicarbonate.

It seems that in most cases of acute anuria these measures will be sufficient to keep the patient alive. Occasionally more drastic measures may be necessary. The latter is often the case in patients with anuria who have been treated with large amounts of fluid and salts. Under these circumstances, the artificial kidney, peritoneal dialysis, intestinal irrigation and exsanguinotransfusion have been used, occasionally with success. All these drastic methods have their advantages and disadvantages and should only be employed if strict indications exist.

At the time of this writing eleven uremic patients have recovered after use of the artificial kidney, twenty-one after peritoneal dialysis. No method is available which permits a satisfactory intestinal irrigation and prevents dangerous changes in the electrolyte content of the blood.

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